



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

Address: COMMISSIONER FOR PATENTS

P.O. Box 1450

Alexandria, Virginia 22313-1450

www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,739	04/09/2004	Gabor Tigyi	UTRF013	2451
41546	7590	03/21/2008		
DONNA J. RUSSELL 1492 ANTHONY WAY MT. JULIET, TN 37122			EXAMINER OLSON, ERIC	
			ART UNIT 1623	PAPER NUMBER
			MAIL DATE 03/21/2008	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/821,739

Applicant(s)

TIGYI ET AL.

Examiner

Eric S. Olson

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 January 2008.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3, 4, 12, 13 and 19-24 is/are pending in the application.
4a) Of the above claim(s) 3, 4, 12 and 13 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 19, 21, 22 and 24 is/are rejected.
7) ☒ Claim(s) 20 and 23 is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

Detailed Action

This office action is a response to applicant's communication submitted January 23, 2008 wherein claims 1, 2, 5-11, and 14-18 are cancelled and new claims 19-24 are introduced. This application claims benefit of provisional application 60/462274, filed April 11, 2003.

Claims 3, 4, 12, 13, and 19-24 are pending in this application.

Claims 19-24 as amended are examined on the merits herein.

Applicant's amendment, submitted January 23, 2008, with respect to the rejection of instant claims 5, 6, 8, 14, 15, and 17 under 35 USC 112, second paragraph, for reciting the indefinite phrase, "analog of lysophosphatidic acid," has been fully considered and found to be persuasive to remove the rejection as the rejected claims have been cancelled and the new claims do not recite the indefinite phrase. Therefore the rejection is withdrawn.

Applicant's amendment, submitted January 23, 2008, with respect to the rejection of instant claims 1, 2, 5-11, and 14-18 under 35 USC 112, first paragraph, for lacking enablement for a method of has been fully considered and found to be persuasive to remove the rejection as the rejected claims have been cancelled and the new claims do not recite a method of prevention. Therefore the rejection is withdrawn.

The following rejections of record in the previous office action are maintained:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19, 21, 22, and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a therapeutic method comprising administering certain specific PPAR- γ antagonists such as those recited in claim 7, does not reasonably provide enablement for a method comprising administering any compound whatsoever that inhibits signaling through PPAR γ . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApts 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The claimed invention is a method of treating a disorder by administering a pharmaceutical compound.

The state of the prior art: Interaction of lysophosphatidic acid with its receptors is known in the art to affect cell proliferations including that taking place in atherosclerosis and neointima formation. Certain specific compounds are known in the art to disrupt this interaction and interfere with cell proliferation. However, the prior art does not include a complete, exhaustive listing of every compound that is a PPAR γ antagonist. Based on the number of uncharacterized compounds in existence, the total number of PPAR γ antagonists is likely to be very large.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: The design of ligands to receptors is unpredictable. A compound similar to an existing antagonist can easily turn out to not bind the receptor, or to bind as an agonist. Predicting the activity of a novel compound not similar to any existing ligand is even more difficult, if not impossible.

Furthermore, the art of organic synthesis of novel compounds is complex. For a novel, complex compound to be synthesized, one skilled in the art must develop and optimize a synthetic method by trial and error, involving unpredictable experimentation.

The Breadth of the claims: The claimed invention is very broad, encompassing methods comprising administering any chemical substance whatsoever. These substances include organic small molecules, polynucleotides, polypeptides,

oligosaccharides, inorganic complexes, and any other compound that could reasonably be administered to a living subject.

The amount of direction or guidance presented: The instant specification provides a rationale for concluding that PPAR γ antagonists will disrupt the formation of neointima, and furthermore discloses a number of specific PPAR γ antagonists. The specification does not provide an exhaustive list of all possible PPAR γ antagonists or of any method of predicting the full range of said antagonists.

The presence or absence of working examples: No working examples are provided of actual methods for treating disease.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as the discovery of a broad class of compounds. See MPEP 2164.

The quantity of experimentation necessary: One of ordinary skill in the art, in order to practice the claimed invention with the full range of PPAR γ antagonists beyond the meager number disclosed in the specification would be required to test potential compounds *in vivo* to determine whether a particular compound is useful as a PPAR γ antagonist. According to the 2006 Chemical Abstracts catalog, (Reference included with PTO-892) The Chemical Abstracts Registry contains entries for approximately 26 million compounds, all of which are potentially included in the claimed invention if they happen to have PPAR γ antagonist activity. For most compounds, it is unknown whether they are or are not useful as PPAR γ antagonists. Gathering this data for every

compound known to man would involve *in vitro* screening of an enormous diversity of chemical compounds for PPAR γ antagonist activity, as well as *in vivo* testing of compounds having this activity involving either human or animal subjects to determine therapeutic utility. *In vitro* testing requires that the compounds to be tested be synthesized and subjected to an appropriate screening method. As described earlier, synthesis of diverse chemical structures requires novel and unpredictable experimentation in order to develop suitable synthetic methods. *In vivo* animal experiments include, along with induction of the disease state, administration of the potential pharmaceutical compound and collection and analysis of data, additional burdens associated with compliance with animal welfare regulations, care, feeding, and other maintenance of the animals, dissection of dead animals to collect data, and disposal of dead animals after the protocol is finished. Human tests impose even greater ethical and regulatory burdens, as well as additional difficulty locating subjects. Because of the unpredictability of the art and the lack of comprehensive working examples covering any significant portion of the total number of potential PPAR γ antagonists, these animal experiments would need to be repeated hundreds of times, and involve the maintenance, killing, dissection, and disposal of thousands of experimental animals, to establish the activity or lack thereof of every possible adenosine A_{2A} antagonist, thus presenting an a burden of undue experimentation to anyone practicing the invention with the full range of PPAR γ antagonists claimed.

Genentech, 108 F.3d at 1366, states that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent

protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the breadth of the claims and the unpredictability of the art, Applicants fail to provide information sufficient to practice the claimed invention for all possible compounds that inhibit signaling through PPAR γ .

Response to Argument: Applicant's arguments, submitted January 23, 2004, with respect to the above ground of rejection, has been fully considered and not found to be persuasive to remove the rejection. Applicant argues that the claims are fully enabled because the specification and the art provide various examples of compounds that inhibit PPAR γ signaling, and that furthermore Applicant is not required to provide an exhaustive list of each and every possible chemical substance that can inhibit PPAR γ signaling. Applicant further argues that the requirement that one skilled in the art would have to gather PPAR γ inhibition data for every compound known to man is an excessive burden to require for the invention to be enabled. However, the rejected claims are not drawn to a method using certain well-defined compounds, but rather to one using an extremely broad, open-ended class of compounds defined only by their biological function and sharing no common structural identity. In such a case the scope of the claims really does include any possible chemical compound that happens to have PPAR γ inhibitory activity. There is no way to know what the limits of this broad, ill-defined class of compounds are except by assaying a representative sample of all compounds which could reasonably happen to have this activity. True, Applicant has

provided a few examples of compounds that meet this description, but the examples provided come nowhere close to being a representative sample of all of the PPAR γ inhibitors in existence. Therefore known examples of PPAR γ inhibitors do not serve to enable the claimed invention.

Applicant further states that the experimentation needed to screen any arbitrary number of compounds for a given biological activity is not undue. However, when the scope of the invention includes every compound in existence having a particular activity, then this supposedly routine experimentation will include obtaining and testing a massive library of unrelated chemical compounds, many of which are exotic and cannot be obtained commercially or synthesized without expending undue and unpredictable effort developing a synthetic strategy. The ordinary, predictable research mentioned by Applicant involves screening a specific chemical library containing certain definite compounds that can be obtained without undue experimentation. The purpose of these studies is to generate a limited number of lead compounds for further development. No one even tries to exhaustively test every conceivable compound as is required by the instant claims. The reasonable detail cited by Applicant that has been provided by the disclosure serves only to indicate that certain previously known compounds have the additional utility of being useful as therapeutic agents to inhibit neointima formation. The disclosure does not in any way serve to expand the currently available knowledge as to the scope of compounds which exhibit these activities.

In short, the instant claims include the unusual feature of encompassing an open-ended class of functionally defined compounds, most of which are not currently known

in the art. Therefore they bear little or no resemblance to the scope of currently known PPAR γ inhibitors or to the actual therapeutic methods included in the disclosure as originally filed. For these reasons the rejection is maintained and made **FINAL**.

Conclusion

Claims 19, 21, 22, and 24 are rejected. Claims 20 and 23 are objected to for depending from a rejected base claim but would be allowable if rewritten in independent form incorporating all of the limitations of the rejected base claim and any intervening claims. **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S Olson/
Examiner, Art Unit 1623
3/11/2008

/Shaojia Anna Jiang, Ph.D./
Supervisory Patent Examiner, Art Unit 1623